8.0 QUALITY OF DATA REVIEWED

8.1 Extent of Adherence to GLP Guidelines

Ideally, all data supporting the validity of a test method should be obtained and reported in accordance with GLP guidelines, which are nationally and internationally recognized rules designed to produce high-quality laboratory records. GLPs provide a standardized approach to the reporting and archiving of laboratory data and records, and information about the test protocol, to ensure the integrity, reliability, and accountability of a study (U.S. EPA, 2001, 2002; FDA, 2002). Based on the information provided in the reports included in this BRD, the only *in vitro* ER TA studies conducted in compliance with GLP guidelines were those performed by Xenobiotic Detection Systems, Inc.

8.2 Assessment of Data Quality

Formal assessments of data quality, such as quality assurance audits, generally involve a systematic and critical comparison of the data provided in a study report or published paper to the laboratory records generated during the study. No attempt to formally assess the quality of the data was performed for this BRD. The published and submitted data on the TA of ER-inducible genes were limited, in most reports, to the response of the substance in the test system relative to 17β-estradiol or to a vehicle control, and to a lesser extent, EC_{50} values, and rates of enzyme activity. A number of studies used cell proliferation as a surrogate endpoint for TA; some of these studies used 17β-estradiol or another potent estrogen as a reference estrogen. Auditing these reported data and values would require obtaining the original data for each study, which are not readily available.

An informal assessment of the *in vitro* ER TA publications and the two submitted reports revealed limitations that complicate interpretation of the ER TA data (**Appendix D**):

- *Various formats used to report study results*: The data from the studies were reported in a variety of formats. Yeast-based reporter gene studies reported test results in Miller Units (A_{420}/min/mL cells/OD_{600}), potency ratios (EC_{50} test substance/EC_{50} 17β-estradiol), β-galactosidase activity, percent maximal response, and relative potency (EC_{50} 17β-estradiol/ EC_{50} test substance x 100). Studies using reporter genes in mammalian cell lines reported results as fold induction or increase, relative potency ratios, relative agonistic activity, EC_{50}

values, concentration-response curves, and rates of enzyme activity. Cell proliferation studies reported results as cell number, foci/cm^2, EC_{50} values, cell growth relative to hormone free control, increase in protein or DNA content, and fold increase in cell proliferation relative to vehicle control. The values reported were, as a rule, obtained from different protocols, and against different standards, and there typically was little or no information regarding the concentrations of ER or reporter gene constructs. These factors make a quantitative analysis of assay reliability difficult.

- *Large number of substances tested in only one laboratory*: Relatively few of the substances included in this BRD have been tested by more than one laboratory using the same protocol. Therefore, the interlaboratory reproducibility of the results for many of the substances cannot be determined.
- *Large number of substances without information regarding within-laboratory reproducibility:* There is often no information in the published scientific articles as to the number of replicates or repeat experiments performed. Therefore, the within-laboratory repeatability of many of the test results cannot be determined.
- *Insufficient methodology information*: Many of the published studies contained limited details about the specific test protocols, cells, and vectors used. In some cases, methods were reported as being "performed as previously described," and in many of these cases the cited publication either referenced another publication for experimental details, or was not relevant to the particular protocol. Thus, for some studies, it was not possible to determine the actual protocol used to produce data.
- *Inconsistent nomenclature of test substances:* Most studies did not provide CASRNs for the substances tested, or used a unique chemical nomenclature, which in some cases made unequivocal identification of the test substance difficult.

8.3 Quality Control Audit

A quality control (QC) audit of the *in vitro* ER TA database provided in **Appendix D** was conducted. The data in the database was checked against the original sources and entry errors were corrected.